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SUPERIOR COURT OF THE STATE OF CALIFORNIA

FOR THE COUNTY OF LOS ANGELES, CENTRAL DISTRICT

VINCENT TSAI, an individual; OSCAR RODRIGUEZ, an individual; ENRIQUE IRIBE, an individual; MOHAMED BINA, an individual; SHAYNE LAMONT, an individual; and PROTECTION FOR THE EDUCATIONAL RIGHTS OF KIDS, a California non-profit corporation, Plaintiffs, vs. THE COUNTY OF LOS ANGELES, a municipal entity, Defendant.	Case No. 21STCV36298 Assigned for all purposes to the Hon. Gail Killefer **THIRD AMENDED COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF** Trial Date: May 2, 2023 FSC: April 25, 2023 Complaint filed: October 1, 2021

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Plaintiffs Vincent Tsai et al. ("Plaintiffs") allege as follows:

INTRODUCTION

1. In August 2021, the Los Angeles County Board of Supervisors ordered all LA County employees to get the Covid-19 vaccine to keep their jobs. It did not have the authority to do that as Covid-19 is not a workplace risk that employers—even government employers—have the power to regulate.

2. Even if has the authority to mandate the Covid vaccines, the County must show that they prevent people from transmitting Covid-19. That is the only plausible "public health" reason for mandating the shots. But the County cannot show that. The Covid vaccines do not prevent a person from being infected with, or spreading, the novel coronavirus. Public health officials around the world acknowledge that. That is why millions of vaccinated people continue to get infected with Covid. Thus, the County's vaccine mandate does not serve its stated purpose of preventing infection. The most the shots can do is protect against severe illness or death, but that is a private health matter not a public one or a workplace risk that employers should be allowed to regulate. Indeed, state and federal laws prohibit employers from making employment decisions based on a person's health condition, including an immunological condition.

3. There is also mounting evidence that the Covid-19 shots may not be safe for some people, as hundreds of thousands of adverse reactions have been reported to the Department of Health and Human Services, many in healthy people. And, at this point, being "fully vaccinated" against Covid-19 requires at least one booster shot, which many County employees do not want, even if they got the initial shot.

4. Moreover, the County mandate is unconstitutional because it violates county employees' state constitutional right to privacy, a right the California Supreme Court has construed to protect an individual's right to bodily autonomy—the freedom to choose, without interference, what to do with one's own body.

5. The County said it would fire any County employees who refused to get the Covid shots. Thousands of County employees did not comply. Some, like Plaintiff Shayne Lamont, have

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already been fired. Others will be fired soon. Thousands more got the first dose of the vaccine but do not want the booster shots. They could lose their jobs if the County mandates all the recommended booster shots.

6. The County said it would honor religious and medical exemptions to the vaccine mandate. But, in practice, that has not happened. Some County departments have denied all requests for exemptions. Others granted them. Some granted some but denied others. There is no rhyme or reason to this practice and the results often depend on which workers have the most vocal advocates.

7. The County has often claimed that its mandate is not coercive. It is not forcing people to get the Covid shot. The unvaccinated just can't work for the County. That misses the point. The County intended its mandate to be coercive, to accomplish its policy of universal vaccination as the way to end the Covid pandemic. That coercion violates county employees' right to bodily autonomy, the freedom to choose whether to get the shot or not. It is also arbitrary. While the County tries to fire those people who did not get any of the Covid shots, it has not taken any action against people who got the first shots but who do not want the boosters. There is little, if any, immunological difference between the unvaccinated and the un-boosted and thus there is no reason to treat those classes of people differently.

8. PERK is a non-profit organization that advocates for civil rights, bodily autonomy, medical freedom and other rights, with a particular focus on children and parental rights. PERK joined this lawsuit because of the devastating effect the County's unlawful mandate would have on children and families in Los Angeles. County residents cannot afford to lose thousands of public employees. They would be unable to obtain critical public services, including social services that kids and families depend on. The County's unlawful actions have also exposed it to hundreds of wrongful termination and discrimination lawsuits. Those will cost millions of dollars in taxpayer money to defend and resolve. Thus, PERK has a beneficial interest in the relief sought in this Complaint. It also has standing under the more liberal public interest standing rules that govern constitutional cases in state court.

9. Plaintiffs Tsai, Rodriguez, Iribe, Bina and Lamont are County employees, some of

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whom were ordered to comply with the vaccine mandate but have not complied. Mr. Lamont has already been fired. He did not receive any of the procedural protections he is entitled to under the Due Process Clause and the California Supreme Court's decision in *Skelly v. State Personnel Board* and he had a pending request for a religious exemption, which his supervisors in the County Department of Health ignored and denied only after they fired him.

10. Plaintiffs seek declaratory and injunctive relief to declare the County's vaccine mandate unlawful because it is arbitrary and capricious and because the County acted arbitrarily and capriciously in issuing it and by aggressively going after employees who did not get the first Covid shot while doing nothing to County employees who got the first shot but did not get any of the booster shots. They seek to enjoin the County from continuing to enforcing the mandate against any County employees.

PARTIES, JURISDICTION AND VENUE

11. PERK is a 501(c)(3) non-profit organization formed under the laws of the State of California that advocates for civil rights issues, bodily autonomy, medical freedom and other rights, with a particular focus on children and parental rights. PERK has dedicated considerable resources to advocating for individual rights during the Covid-19 pandemic and thus has a beneficial interest in the relief sought in this action.

12. Plaintiff Tsai is a County employee who was ordered to comply with the vaccine mandate or be fired. He works for the Los Angeles County Sheriff's Department.

13. Plaintiff Rodriguez is a County employee who was ordered to comply with the vaccine mandate or be fired. He works for the Los Angeles County Sheriff's Department.

14. Plaintiff Iribe is a County employee who was ordered to comply with the vaccine mandate or be fired. He works for the Los Angeles County Probation Department. He was suspended for four days, without pay, for not complying but that suspension was later rescinded.

15. Plaintiff Bina is a County employee. He works for the Los Angeles County Department of Sanitation. He has not yet been ordered to comply with the vaccine mandate but could be in the future.

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16. Plaintiff Shayne Lamont is a County employee who was fired for not complying with the County's employee vaccine mandate. He worked for the Los Angeles County Department of Public Health.

17. Plaintiffs Tsai, Rodriguez, Iribe, Bina and Lamont are referred to collectively as the "Individual Plaintiffs."

18. The County of Los Angeles is a municipal organization formed under the laws of the State of California. The vaccine mandate was issued by Supervisor Hilda Solis and ratified by a vote of the County Board of Supervisors. Thus, it represents an official policy of Los Angeles County.

19. Venue exists in Los Angeles County under sections 393(b) and 394(a) of the Code of Civil Procedure because the Complaint alleges claims against a municipal entity that exists and operates in Los Angeles County and because the mandate's effects will be felt here.

FACTUAL ALLEGATIONS

20. In early 2020, health officials discovered a novel coronavirus circulating in Wuhan, China. They named the illness caused by the virus "Covid-19."

21. Though nobody knew it at the time, the Covid-19 pandemic would lead to unprecedented restrictions on liberty. Many of the restrictions started in California.

22. During 2020, at the urging of then President Donald Trump, several pharmaceutical companies began developing experimental treatments to mitigate the effects of Covid-19 and, potentially, reduce its spread.

23. The Covid-19 shots were so controversial that many Democratic Party politicians, including then candidates Joe Biden and Kamala Harris, would not commit to taking them. President-elect Biden also said that he would not mandate that Americans get the Covid shots, a recognition of the robust privacy rights that Americans now enjoy under the federal and state constitutions.

24. By the summer of 2021, tens of millions of Americans had taken the Covid-19 shots anyway, including more than half of adults in California. But Covid-19 had not disappeared. That should not have surprised anybody. Public health officials have repeatedly said that eliminating a

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respiratory virus is impossible once it starts spreading in the community. According to one prominent epidemiologist, speaking to *Nature*: "Eradicating this virus right now from the world is a lot like trying to plan the construction of a stepping-stone pathway to the Moon. It's unrealistic."

25. Thus, anyone can still contract and spread the Covid-19 virus, including people who have received one of the Covid-19 shots. The shots do not prevent infection. They do not prevent an infected person from spreading the virus. The most they can do is reduce the severity of an infected person's symptoms, although even that is speculative.

26. Public health officials knew this all along. For example, the Department of Health and Human Services' Centers for Medicare and Medicaid Services ("CMS") stated last fall in the *Federal Register* that "the duration of vaccine effectiveness in preventing COVID-19, reducing disease severity, reducing the risk of death, and the effectiveness of the vaccine to prevent disease transmission by those vaccinated are not currently known."

27. This was not an isolated comment. Moderna and Pfizer executives have both conceded that their shots, unlike others that have helped eradicate diseases like polio and smallpox, have little known long-term benefit.

28. Hopes that the Covid shots would end the pandemic were dashed last winter, as the Omicron variant of Covid-19 spread throughout the world, infecting millions of vaccinated people. The Centers for Disease Control finally conceded in February 2022 that "anyone with Omicron infection can spread the virus to others, even if they are vaccinated or don't have symptoms." A true and correct copy of this report is attached to this Complaint as **Exhibit "B."** A true and correct copy of the CDC's current guidance regarding the vaccines, updated as of June 23, 2022, is attached as **Exhibit "C."**

29. The booster shots that Pfizer and Moderna developed did not help, either. Indeed, Anthony Fauci recently contracted Covid-19 despite getting the first Covid shots plus two boosters. The Covid vaccines have proven to be so ineffective that *The Wall Street Journal* recently ran an article titled "Can We Develop a Covid-19 Vaccine that Lasts?" More than 82 million doses of the shots have been discarded due to waning demand.

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30. Studies have also revealed potential serious side effects from the Covid-19 shots. For example, a British report that examined data from more than 42 million people found an increase in myocarditis with mRNA vaccines like the Covid-19 shots that increased with each additional shot, including the booster shots. That report's authors concluded that "[a]n association between Covid-19 infection and myocarditis was observed in all ages for both sexes." A true and correct copy of this report is attached as **Exhibit "D."** According to another report, a recent study from Sweden found that the "messenger RNA from Pfizer's COVID-19 vaccine reportedly can enter human liver cells and be converted into DNA, contrary to what the CDC has said." A true and correct copy of this report is attached as **Exhibit "E."**

31. This growing body of evidence confirms what many public health officials said all along. As former Yale professor Dr. David Gortler put it: "Vaccines are one of the most important inventions in human history, having saved millions of lives. That does not mean every person should get every vaccine. Also, like every drug out there, it is critically important to quickly detect and report safety problems." Dr. Gortler concluded that the Covid-19 shots are "clearly no longer effective, and [are] potentially causing additional illness and death." A true and correct copy of Dr. Gortler's comments is attached as **Exhibit "F."**

32. This evidence has been available for months. But some government officials decided during the summer of 2021 that universal vaccination was the only way to end the pandemic. To accomplish that, they mandated that people get the Covid-19 shot to keep their jobs. To that end, on August 4, 2021, Hilda Solis, then the honorary chair of the Los Angeles County Board of Supervisors, issued an executive order to "[e]stablish a mandatory vaccination policy, effective immediately, which requires all County employees to provide proof of full vaccination by October 1, 2021 …." A true and correct copy of this order is attached as **Exhibit "A."**

33. The County's vaccine mandate was unprecedented. The County had never required that employees get a shot to keep their jobs, even during a pandemic. The County had never fired an employee for declining a vaccine, or any medical treatment, either. To the contrary, state and federal law prohibits employers from making employment decisions based on an individual's personal

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health matters, including an immunological condition (which a person's vaccination status clearly qualifies as). It is unlawful under state and federal law to even ask about these matters.

34. Although characterized as an "executive order," Ms. Solis is not an executive officer. She chaired the Board of Supervisors last year, an honorary position. On information and belief, Ms. Solis did not consult with the other supervisors before issuing the August 4 order. Her order did not include any scientific explanation for the mandate but relied on generalized assertions and political statements, such as President Biden's vow to force the shots on federal workers (a mandate that has been stayed nationwide and which may be vacated by the Supreme Court).

35. Ms. Solis based her August 4 order on section 8634 of the Government Code, part of the California Emergency Services Act, which states: "During a local emergency the governing body of a political subdivision, or officials designated thereby, may promulgate orders and regulations *necessary* to provide for the protection of life and property, including orders or regulations imposing a curfew within designated boundaries where necessary to preserve the public order and safety. Such orders and regulations and amendments and rescissions thereof shall be in writing and shall be given widespread publicity and notice." (Emphasis added.)

36. On August 10, 2021, the Board of Supervisors ratified Ms. Solis' order, making it an official County policy. On information and belief, the Board held little debate about the mandate, which affects 110,000 people. It did not consider the evidence that the Covid-19 shots do not prevent infection or reduce the virus' spread. It did not consider the benefits of having recovered from prior infection. It did not consider the potential side effects, a legitimate reason for anybody to consider not getting them. It did not consider statements from people like Dr. Gortler who, while acknowledging the potential benefits, said there is no need for everybody on Earth to get every vaccine.

37. Indeed, the Board did not gather any evidence about the effectiveness or necessity of the shots. The supervisors described universal vaccination as a *fait accompli*, with Supervisor Holly Mitchell saying: "While it may be tempting to provide more flexibility for people not to be vaccinated and be tested instead, this would just delay the inevitable." Supervisor Solis couched the

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decision in political terms, saying that the "unvaccinated" had "refuse[d] to do their part" to help end the pandemic.

38. This decision-making process was arbitrary and capricious, as the Board, like Ms. Solis, failed to engage in any legitimate fact-finding. Instead, the Board had a pre-determined policy position—universal vaccination—and simply set forth findings to justify it.

39. Moreover, since issuing the mandate, the Board has ignored evidence that shows the ineffectiveness and potential side effects from the Covid-19 shots. Ignoring evidence that undermines the government's predictions about a given policy is quintessentially arbitrary and capricious. California law prohibits it, especially when the government's decision impacts people's constitutional rights.

40. The Board also did not account for the many County employees who received the Covid-19 shot but did not want to disclose their medical history to their employer. Their concerns have merit, as they have a right under the California Constitution to protect the privacy of this information. They also have a right to bodily autonomy that prohibits the government from interfering with their freedom to choose what they do with their bodies. These rights are found in Article I, section 1 of the California Constitution, added by voters in 1972 to provide privacy rights that go far beyond the federal Constitution.

41. The County has invaded these privacy interests in unreasonable and unnecessary ways, including by forcing employees to upload their private health information into the Fulgent app, the technology the County and other government agencies in California use to track individuals' medical status. Plaintiffs are informed and believe, and on that basis allege, that the Fulgent app gathers genetic and medical data and cross-references and links the same through blockchain technology to individuals' assets, property, residence, credit and financial data. It stores the same and shares said data with other data mining companies thus invading, with the imprimatur and contractual assistance of the County, Plaintiffs' right to privacy under the California Constitution.

42. The County said the vaccine mandate was necessary to protect life and property. But by allowing some unvaccinated employees to work for the past year—sometimes while testing and

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wearing masks, sometimes not—the County has shown that the mandate is *not* necessary. Moreover, at this point, there is little, if any, immunological difference between people who did not get any of the Covid shots and people who got the original shots but did not get the boosters. Real-world evidence shows that. For example, Walgreens has been collecting data on Covid infections for months. It has consistently found the unvaccinated to test positive at the same, or even a lesser, rate than people who have taken one or more of the Covid shots. Its data from the last week of June showed that people who took just the original two doses of the vaccine more than five months ago to be testing positive more than 38 percent of the time. *See* https://www.walgreens.com/businesssolutions/covid-19-index.jsp (last visited July 8, 2022).

43. Tens of thousands of county employees fall into this "vaccinated but un-boosted" category. But while the County aggressively targets the unvaccinated for not protecting themselves from Covid, it has not taken any action against its un-boosted employees. Nor will it. The unvaccinated group is small enough to replace. The County could not function if it fired tens of thousands of un-boosted employees.

44. Los Angeles has been in a "state of emergency" related to Covid-19 for more than two years. We have learned an unprecedented amount of information about Covid-19 during that time, including information about how the virus spreads and who is most vulnerable to it. Thus, Covid-19 is no longer a condition of extreme peril that requires emergency rule to handle. The County must comply with its duty to terminate a state of emergency "at the earliest possible date that conditions warrant." That date has passed.

45. This was true when Plaintiffs filed this case last fall. It has not changed. If anything, the pandemic's dissipation during the past six months—with a highly contagious but less serious strain—has obviated any need for the County's state of emergency and vaccine mandate. Even Dr. Fauci said that America is "out of the pandemic phase." NPR, "Here's why Dr. Fauci says the U.S. is 'out of the pandemic phase'" (Apr. 28, 2022), https://www.npr.org/2022/04/27/1094997608/fauci-us-pandemic-phase-covid-19. Moreover, we now have undisputed evidence that the Covid vaccines do not prevent infection or spread and thus cannot end the pandemic. At most, they help reduce the

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symptoms of Covid-19. But governments cannot compel competent adults to get a shot they do not want simply because it may reduce the severity of their illness, just as they cannot force people to eat their fruits and vegetables or exercise four times per week, both things the CDC recommends.

46. This is not a trivial issue. Many of the employees affected by the County's vaccine mandate have spent decades working for the County. They deserve to be heard.

47. It is also time for courts to exercise meaningful judicial review, to apply the law evenhandedly and to prevent governments from conditioning an end to the pandemic on the livelihoods of public employees who want to make their own health decisions, free from their employer's interference. Plaintiffs bring this action to protect those rights and to enjoin any further enforcement of the County's vaccine mandate.

FIRST CAUSE OF ACTION

(Declaratory and Injunctive Relief under Cal. Emergency Services Act to Compel the County to Terminate the Local Covid-19 Emergency)

48. Plaintiffs incorporate the preceding paragraphs of this Complaint as though set forth fully herein.

49. The County adopted and has enforced the employee vaccine mandate pursuant to its powers under the California Emergency Services Act, which is codified in sections 8550 *et seq.* of the California Government Code. The existence of the local emergency was the sole basis for adopting and enforcing the mandate. Thus, if the County ends the state of emergency, either voluntarily or by a court order, the vaccine mandate will also terminate.

50. The term "emergency" has a specific meaning under the Emergency Services Act. "'Local emergency' means the duly proclaimed existence of conditions of disaster or of extreme peril to the safety of persons and property within the territorial limits of a county, city and county, or city, caused by conditions such as air pollution, fire, flood, storm, epidemic, riot, drought, cyberterrorism, sudden and severe energy shortage, deenergization event, plant or animal infestation or disease, the Governor's warning of an earthquake or volcanic prediction, or an earthquake, or other conditions, other than conditions resulting from a labor controversy, which are or are likely to

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be beyond the control of the services, personnel, equipment, and facilities of that political subdivision and require the combined forces of other political subdivisions to combat ….” Cal. Gov’t Code § 8558(c)(1).

51. The emergency cannot last forever. The Emergency Services Act requires that local officials “review the need for continuing the local emergency at least once every 60 days until the governing body terminates the local emergency.” Cal. Gov’t Code § 8630(c). (The Governor has exempted all local officials from this duty by repeatedly extending the statewide state of emergency, a decision that is being challenged in another lawsuit.) Moreover, in exchange for its broad delegation of power, the Act requires that the emergency end as soon as possible. “The governing body *shall* proclaim the termination of the local emergency at the earliest possible date that conditions warrant.” *Id.* § 8630(d) (emphasis added). This is a mandatory duty.

52. The County issued the local state of emergency in March 2020, when Covid-19 was a novel virus that doctors did not know how to treat and which public health officials said could lead to a surge of sick patients that would overwhelm California’s health care system, causing millions of unnecessary deaths. That was the condition of “extreme peril,” the sudden and unexpected necessity, that justified the proclamation of a local state of emergency.

53. Plaintiffs contend that those conditions of extreme peril no longer exist. To the contrary, public health officials have obtained an unprecedented amount of knowledge about the virus that causes Covid-19. They know how it spreads. They know how to treat it. They know who is most vulnerable to it. Thus, Plaintiffs contend that the County has a duty to terminate the local emergency related to Covid-19. In the alternative, Plaintiffs contend that the County has acted arbitrarily and capriciously in refusing to terminate the emergency and in extending the emergency indefinitely without conducting a good-faith review of the need for it.

54. On information and belief, the County contends that it does not have a duty to terminate the Covid-19 emergency and that it has not acted arbitrarily and capriciously by refusing to terminate the emergency or by failing to review the need for it every 60 days.

55. Plaintiffs desire a judicial declaration that the County has a duty to terminate the local

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emergency related to Covid-19 and that the County has violated that duty by failing and refusing to terminate the state of emergency.

56. A judicial determination of these issues is necessary and appropriate because such a declaration will clarify the parties' rights and obligations, permit them to have certainty regarding those rights and potential liability, and avoid a multiplicity of actions.

57. The County's actions have harmed Plaintiffs and those they represent, as alleged above.

58. Plaintiffs have no adequate remedy at law and will suffer irreparable harm if the Court does not order the County to terminate the Covid-19 state of emergency. Thus, they seek preliminary and permanent injunctive relief mandating that action and enjoining the County from issuing any further orders pursuant to the Emergency Services Act and under the Covid-19 emergency proclamation.

59. This action serves the public interest, justifying an award of attorneys' fees under section 1021.5 of the California Code of Civil Procedure.

SECOND CAUSE OF ACTION

(Declaratory and Injunctive Relief under Cal. Emergency Services Act for *Ultra Vires* Action)

60. Plaintiffs incorporate the preceding paragraphs of this Complaint as though set forth fully herein.

61. The Emergency Services Act gives local officials the power to "promulgate orders and regulations *necessary* to provide for the protection of life and property," in the affected area during a state of emergency. Cal. Gov't Code § 8634 (emphasis added).

62. Plaintiffs contend that the vaccine mandate exceeds the County's authority under this law for five reasons.

63. First, the mandate is not necessary to protect life or property, as the Covid shots do not prevent infection or the spread of Covid-19. They *may* reduce the severity of an infected person's symptoms but that is speculation and speculation does not equal necessity. Moreover, necessity means that there are no other alternatives. County employees have many ways to protect

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themselves from getting seriously ill or dying from Covid-19. Indeed, many County employees have an inherently low risk of serious illness and death due to their age and health.

64. Second, reducing the severity of an infected person's symptoms was not the reason the County gave for mandating the Covid shots. It said the shots were necessary because they would prevent infection/spread and would end the pandemic. That is not true. Indeed, in a recent deposition in another case, Dr. George Rutherford, an expert witness for Governor Gavin Newsom, said the pandemic could last another five years, regardless of the availability of vaccines. Thus, the vaccine mandate does not serve the County's stated goal of preventing infection and ending the pandemic.

65. Third, the County has a duty under the Emergency Services Act to narrowly tailor government action to protect individual rights. That requires that any action be the least restrictive means of accomplishing the County's interest. The vaccine mandate is the most restrictive. Combined with its ineffectiveness, this makes the mandate unlawful under the Act.

66. Fourth, if the Covid vaccines were necessary to protect life and property, the County would also require that its employees get all the recommended booster shots (now two boosters and counting) and it would be just as aggressive in targeting un-boosted employees for not protecting themselves from the virus. It has not done that and, on information and belief, does not intend to fire any County employees for not getting the booster shots because there are far too many of them. This disparate treatment of the unvaccinated and the un-boosted is arbitrary and capricious and undermines the purported necessity of the mandate.

67. Fifth, Plaintiffs also contend that the County acted arbitrarily and capriciously in adopting the vaccine mandate in the first place, as it failed to consider evidence of the Covid-19 shots' ineffectiveness, which was already available by August 2021. Instead, the County, through Supervisor Solis, decided to mandate the shots for political reasons (hence the numerous references to President Biden and his proposed mandates in Supervisor Solis' order) and simply set forth findings to justify the decision, while ignoring evidence that undermined its pre-determined decision. That is quintessentially arbitrary and capricious.

68. The County disagrees with these allegations. It contends that it did have the power to

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order its employees to get the Covid-19 shots and that it did not act arbitrarily and capriciously in that process or in its disparate treatment of people who did not get any of the Covid shots compared to those who got the original shots but who did not get the boosters.

69. Plaintiffs desire a judicial declaration that, for the five reasons discussed above, the Covid-19 vaccine mandate exceeds the County's powers under state law. Plaintiffs also seek an order that the County acted arbitrarily and capriciously in adopting and enforcing the mandate.

70. A judicial determination of these issues is necessary and appropriate because such a declaration will clarify the parties' rights and obligations, permit them to have certainty regarding those rights and potential liability, and avoid a multiplicity of actions.

71. The County's actions have harmed Plaintiffs and those they represent.

72. Plaintiffs have no adequate remedy at law and will suffer irreparable harm if the Court does not enjoin the County from enforcing the unlawful vaccine mandate. Thus, Plaintiffs seek preliminary and permanent injunctive relief for such an order.

73. This action serves the public interest, justifying an award of attorneys' fees under section 1021.5 of the California Code of Civil Procedure.

THIRD CAUSE OF ACTION

(Declaratory and Injunctive Relief under Article I, section 1 of Cal. Constitution by Individual Plaintiffs)

74. Plaintiffs incorporate the preceding paragraphs of this Complaint as though set forth fully herein.

75. The Individual Plaintiffs are employed by the County. They have not taken the Covid-19 shots. They object to the County's efforts to control their personal health decisions and object to being compelled to turn over their private medical information to the County as a condition of their employment. They also object to being forced to upload their private medical information through the Fulgent app.

76. Individuals have a right to privacy under the California Constitution. This state law privacy right, which was added by voters in 1972, is far broader than the right to privacy that exists

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under the federal Constitution. It is the broadest privacy right in America.

77. Bodily autonomy means the freedom to choose what to do with one's own body, free from interference. It is related—but not identical—to the right to bodily integrity, which prohibits compulsory medical procedures.

78. In *Hill v. National Collegiate Athletic Association*, 7 Cal.4th 1, 39-40 (1994), the California Supreme Court described the elements needed to plead a claim under Article I, section 1 of the California Constitution: "(1) a legally protected privacy interest; (2) a reasonable expectation of privacy in the circumstances; and (3) conduct by defendant constituting a serious invasion of privacy." *Id.*

79. ***Legally protected privacy interest.*** Bodily autonomy means the freedom to choose what to do with one's own body, free from interference. The California Supreme Court has interpreted the California Constitution's privacy clause to protect both this right and the right to informational privacy. *See Conservatorship of Wendland*, 26 Cal.4th 519, 530-32 (2001) (citing cases and describing right to bodily autonomy as "basic and fundamental"); *see also Coshow v. City of Escondido*, 132 Cal. App. 4th 687, 710 (2005). The County does not dispute this allegation.

80. ***Reasonable expectation of privacy.*** The Individual Plaintiffs' expectation of privacy in their bodily autonomy is reasonable under the circumstances, as the County has never had a vaccination requirement for public employment before now and the County has never disciplined, much less fired, an employee for declining an injection. The only compulsory vaccination laws adopted in California during the past century concerned certain vaccines that *children* need to attend school. Those laws do not undermine the expectation of privacy that *adults* have in their bodily autonomy. Moreover, in 2005, in *Coshow*, the California Court of Appeal identified vaccination as the type of "invasive and highly personalized medical treatments used in cases where the state sought to override a person's freedom to choose and where the Supreme Court has recognized a liberty interest in freedom from such unwanted medical treatment." *Coshow*, 132 Cal. App. 4th at 710. The County's disparate treatment of the un-boosted—respecting their right to decide for themselves whether to get one or more booster shots—provides further evidence that the Individual

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Plaintiffs' expectation of privacy in this matter was reasonable.

81. The County disputes these allegations but, as the Supreme Court explained in *Hill* (and subsequent cases), determining the reasonable of an individual's expectation of privacy in a given matter is a mixed question of law and fact that must be decided on a full record.

82. ***Serious invasion of privacy.*** The Individual Plaintiffs contend that firing county employees who do not get the Covid-19 shot constitutes a serious invasion of the employees' right to bodily autonomy, their freedom to *choose* whether to get the Covid shot, especially given the potential side effects. The County disputes this allegation but it is also a mixed question of law and fact that must be decided on a full record, especially since the County has never had a vaccine mandate of any kind before now and especially because many unvaccinated County employees have worked for the County for decades and stand to lose their pensions and other benefits if they are fired or forced to leave their jobs. And while the County may contend that its mandate is not compulsory—the County is (thankfully) not strapping people down and forcibly injecting them with the Covid shots—it intended the mandate to be coercive, to fulfill the President's policy of universal vaccination to end the Covid pandemic.

83. Moreover, although the County said it would honor religious and medical exemptions to the mandate, it has taken a strict view of such requests and denied most of them or said it cannot accommodate unvaccinated employees. Thus, as a practical matter, County employees must either get the shots against their will or assert an exemption that will likely be denied and which they will have to fight through the administrative process and litigation. These factors, combined with the potential side effects of the shots for those compelled to get them, add up to make the mandate a serious invasion of the Individual Plaintiffs' right to bodily autonomy. And they are buttressed by the requirement that County employees disclose their private health information to their employer, including through the Fulgent app, as alleged above.

84. Although the County contends that its vaccine mandate is justified, that is an affirmative defense that it must be plead and prove and which Plaintiffs dispute.

85. The Individual Plaintiffs desire a judicial declaration that the County's Covid-19

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vaccine mandate is unconstitutional because it violates County employees' right to privacy under Article I, section 1 of the California Constitution.

86. A judicial determination of these issues is necessary and appropriate because such a declaration will clarify the parties' rights and obligations, permit them to have certainty regarding those rights and potential liability, and avoid a multiplicity of actions.

87. The County's actions have harmed the Individual Plaintiffs and other County employees, as alleged above.

88. The Individual Plaintiffs have no adequate remedy at law and will suffer irreparable harm if the Court does not declare the vaccine mandate unconstitutional. Thus, they seek preliminary and permanent injunctive relief enjoining the County from it.

89. This action serves the public interest, justifying an award of attorneys' fees under section 1021.5 of the California Code of Civil Procedure.

PRAYER FOR RELIEF

Wherefore, Plaintiffs pray for relief as follows:

1. For an order declaring the County's Covid-19 vaccine mandate to be invalid because it exceeds the County's power under the Emergency Services Act and the County's police power;

2. For an order declaring that the County has a duty to terminate the local emergency related to Covid-19 and that the County has violated that duty;

3. For an order declaring the County's vaccine mandate unconstitutional because it violates the privacy rights that public employees have under the California Constitution;

4. For injunctive relief enjoining the County from further enforcing the Covid-19 vaccine mandate;

5. For costs and attorneys' fees under section 1021.5 of the Code of Civil Procedure; and

6. For such other relief that the Court determines is just and proper.

Dated: July 12, 2022 JW HOWARD/ ATTORNEYS, LTD.

JW HOWARD/ ATTORNEYS, LTD.
701 B Street, Suite 1725
San Diego, California 92101

By: _____

Scott J. Street
Attorneys for Plaintiffs Vincent Tsai *et al.*

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San Diego, California 92101

PROOF OF SERVICE

I, the undersigned, do declare that I am employed in the county aforesaid, that I am over the age of [18] years and not a party to the within entitled action; and that I am executing this proof at the direction of the member of the bar of the above entitled Court. The business address is:

JW Howard Attorneys LTD
701 B Street, Ste. 1725
San Diego, California 92101

☐ MAIL. I am readily familiar with the business' practice for collection and processing of correspondence for mailing via the United States Postal Service and that the correspondence would be deposited with the United States Postal Service for collections that same day.

■ ELECTRONIC. I am readily familiar with the business' practice for collection and processing of documents via electronic system and said documents were successfully transmitted via One Legal that same day.

☐ PERSONAL. The below described documents were personally served on date below via Knox Services.

On the date indicated below, I served the within:

THIRD AMENDED COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Via One Legal To:

SheppardMullin
1901 Avenue of the Stars, Suite 1600
Los Angeles, CA 90067-6017
Kent Raygor
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I declare under penalty of perjury, under the laws of the State of California, that the foregoing is true and correct and was ***EXECUTED*** on July 12, 2022, at San Diego, CA.

/s/ Dayna Dang
Dayna Dang, Paralegal
dayna@jwhowardattorneys.com

EXHIBIT “A”

EXECUTIVE ORDER OF THE CHAIR OF THE COUNTY OF LOS ANGELES BOARD OF SUPERVISORS FOLLOWING PROCLAMATION OF EXISTENCE OF A LOCAL EMERGENCY DUE TO NOVEL CORONAVIRUS – COVID-19

WHEREAS, on March 4, 2020, the Chair of the Los Angeles County Board of Supervisors ("Board") proclaimed, pursuant to Chapter 2.68 of the Los Angeles County Code ("LACC"), the existence of a local emergency because the County of Los Angeles ("County") was affected or likely to be affected by a public calamity due to conditions of disaster or of extreme peril to the safety of persons and property arising as a result of the novel coronavirus, COVID-19, in the County;

WHEREAS, on March 4, 2020, the Los Angeles County Health Officer issued a declaration of local health emergency due to the occurrence of COVID-19 in the County;

WHEREAS, Government Code Section 8634 and LACC Section 2.68.150 empower the Chair of the Board, during a proclaimed local emergency, to promulgate orders and regulations necessary to provide for the protection of life or property;

WHEREAS, COVID-19 vaccines have been developed to help combat the spread of COVID-19 and prevent people from getting seriously ill from COVID-19;

WHEREAS, the County is now experiencing increased spread due to the highly transmissible Delta variant, which now comprises more than 94% of sequenced cases in the County;

WHEREAS, there are many residents who are not fully vaccinated, including over three million vaccine-eligible residents and one million residents currently ineligible, who are especially vulnerable to the spread of the Delta variant;

WHEREAS, on July 26, 2021, the State of California announced a requirement that all State employees must provide proof of vaccination or submit to at least weekly testing, and encouraged localities and businesses to implement similar programs;

WHEREAS, on July 26, 2021, the California Department of Public Health ("CDPH") issued an order requiring workers in high-risk health care and congregate settings to provide proof of vaccination or submit to at least weekly testing;

WHEREAS, on July 30, 2021, the Los Angeles County Health Officer issued a Health Officer Order, which incorporated by reference, the July 26, 2021 CDPH order requiring workers in high-risk health care and congregate settings to provide proof of vaccination or submit to at least weekly testing;

WHEREAS, on July 26, 2021, the Department of Justice released a Memorandum Opinion stating that Section 564 of the Food, Drug, and Cosmetic Act does not prohibit public or private employers from imposing vaccination requirements for a vaccine that is subject to an emergency use authorization;

WHEREAS, on July 15, 2021, Los Angeles County led by example by being the first in the nation to reinstitute a masking requirement for public indoor settings, which would soon after be emulated in varying degrees by the Centers for Disease Control and Prevention (CDC), the State of California, and other localities across the country;

WHEREAS, on July 29, 2021, President Biden announced that he would direct the Department of Defense to look into how and when they will add the COVID-19 vaccination to the list of required vaccinations for members of the military;

WHEREAS, on July 29, 2021, President Biden announced every federal government employee and onsite contractor will be asked to attest to their vaccination status, and those who do not must comply with testing at least once per week, a masking requirement, physical distancing from other employees and visitors, and restrictions on official travel;

WHEREAS, on June 11, 2021, Governor Newsom issued Executive Order N-08-21, which set a date of October 1, 2021 for public agencies to transition back to public meetings held under the Brown Act;

WHEREAS, the County plans on reopening its buildings to the public on October 1, 2021, and the County has a strong interest in protecting its employees and the public from COVID; and

WHEREAS, pursuant to Government Code section 8634, and in the interest of public health and safety, it is necessary to issue the following order for the protection of life and property.

NOW, THEREFORE, IT IS HEREBY ORDERED THAT:

1. The Chief Executive Officer, in consultation with the Office of County Counsel and the Departments of Human Resources and Public Health, establish a mandatory vaccination policy, effective immediately, which requires all County employees to provide proof of full vaccination by October 1, 2021; and

2. The Chief Executive Officer engage with the County's labor partners regarding the effects of the vaccination policy.

Date: August 4, 2021

Hilda L. Solis
Chair, Los Angeles County Board of Supervisors

EXHIBIT “B”

Centers for Disease Control and Prevention

Omicron Variant: What You Need to Know

Updated Mar. 29, 2022

Free At-Home COVID-19 Tests: Order 8 free tests now so you have them when you need them.

Omicron in the United States

CDC is working with state and local public health officials to monitor the spread of Omicron. As of December 20, 2021, Omicron had been detected in every U.S. state and territory and continues to be the dominant variant in the United States.

Omicron Spread

Learn more about the Omicron variant and its expected impact on hospitalizations.

COVID-19

What We Know about Omicron

CDC has been collaborating with global public health and industry partners to learn about Omicron, as we continue to monitor its course. We are continuing to evaluate how easily it spreads, the severity of illness it causes, and how well available vaccines and medications work against it.

Spread

The Omicron variant, like other variants, is comprised of a number of lineages and sublineages. The three most common lineages of Omicron currently are BA.1, BA.1.1 and BA.2.

The Omicron variant spreads more easily than earlier variants of the virus that cause COVID-19, including the Delta variant. CDC expects that anyone with Omicron infection, regardless of vaccination status or whether or not they have symptoms, can spread the virus to others.

Symptoms

Persons infected with the Omicron variant can present with symptoms similar to previous variants. The presence and severity of symptoms can be affected by COVID-19 vaccination status, the presence of other health conditions, age, and history of prior infection.

Severe Illness

Omicron infection generally causes less severe disease than infection with prior variants. Preliminary data suggest that Omicron may cause more mild disease, although some people may still have severe disease, need hospitalization, and could die from the infection with this variant. Even if only a small percentage of people with Omicron infection need hospitalization

die from the infection with this variant. Even if only a small percentage of people with Omicron infection need hospitalization, a large volume of cases in a community could overwhelm the healthcare system which is why it's important to take steps to protect yourself.

Vaccines

COVID-19 vaccines remain the best public health measure to protect people from COVID-19 and reduce the likelihood of new variants emerging. This includes primary series, booster shots, and additional doses for those who need them.

Current vaccines protect against severe illness, hospitalizations, and deaths due to infection with the Omicron variant. However, breakthrough infections in people who are vaccinated can occur. People who are up to date with their COVID-19 vaccines and get COVID-19 are less likely to develop serious illness than those who are unvaccinated and get COVID-19.

Treatments

Scientists are working to determine how well existing treatments for COVID-19 work. Some monoclonal antibody treatments are less effective against Omicron's BA.2 lineage, but continue to work against BA.1 and BA.1.1 lineages. Other non-monoclonal antibody treatments remain effective against Omicron. Public health agencies work with healthcare providers to ensure that effective treatments are used appropriately to treat patients.

We have the Tools to Fight Omicron

Vaccines

Getting vaccinated and staying up to date with COVID-19 vaccines is the best way to protect yourself and others against the Omicron variant.

- CDC recommends that everyone 5 years and older protect themselves from COVID-19 by getting vaccinated. Everyone ages 12 years and older should stay up to date on their COVID-19 vaccines and get a booster shot when eligible.

Find a COVID-19 vaccine or booster: Search vaccines.gov, text your ZIP code to 438829, or call 1-800-232-0233 to find locations near you.

Masks

Well-fitting masks offer protection against all variants.

- In general, people do not need to wear masks when outdoors.
- If you are sick and need to be around others, or are caring for someone who has COVID-19, wear a mask.
- If the COVID-19 Community Level where you live is
  - Low
    - Wear a mask based on your personal preference, informed by your personal level of risk.
  - Medium
    - If you are at risk for severe illness, talk to your healthcare provider about wearing masks indoors in public.
    - If you live with or will gather with someone at risk for severe illness, wear a mask when indoors with them.
  - High
    - If you are 2 or older, wear a well-fitting mask indoors in public, regardless of vaccination status or individual risk (including in K-12 schools and other community settings).
- If you are at risk for severe illness, wear a mask or respirator that provides you with greater protection.

Testing

Tests can tell you if you have COVID-19. Learn how to get tested.

- Two types of tests are used to test for current infection: nucleic acid amplification tests (NAATs) and antigen tests. NAAT and antigen tests can tell you if you have a current infection.
- Self-tests can be used at home or anywhere, are easy to use, and produce rapid results.
  - If your self-test has a positive result, isolate and talk to your healthcare provider.
  - If you have any questions about your self-test result, call your healthcare provider or public health department.

Individuals can use CDC's COVID-19 Viral Testing Tool to help determine what kind of test to seek.

Your test result will only tell you if you do or do not have COVID-19. It will not tell you which variant caused your infection. Visit your state, tribal, local, or territorial health department's website for the latest local information on testing.

It is important to use **all tools available** to protect yourself and others.

What CDC is Doing to Learn about Omicron

Virus Characteristics

CDC scientists are working with partners to study data and virus samples that may answer important questions about the Omicron variant. CDC will provide updates as new information becomes available.

Variant Surveillance

In the United States, CDC uses viral genomic surveillance to track COVID-19 variants, to more quickly identify and act upon these findings to best protect the public's health. CDC established multiple ways to connect and share viral genomic sequence data being produced by CDC, public health laboratories, and commercial diagnostic laboratories within publicly accessible databases maintained by the National Center for Biotechnology Information (NCBI) and the Global Initiative on Sharing Avian Influenza Data (GISAID). Findings from CDC's variant surveillance are updated on CDC's COVID Data Tracker.

Science Brief: Omicron Lineage Variant(s) (i.e., Pango lineages B.1.1.529, BA.1, BA.1.1, BA.2, BA.3)

On November 24, 2021, South Africa reported the identification of a new COVID-19 variant, B.1.1.529, to the World Health Organization (WHO). B.1.1.529 was first detected in specimens collected on November 11, 2021 in Botswana and on November 14, 2021 in South Africa.

More on the Omicron Lineage Variant(s) (i.e., Pango lineages B.1.1.529, BA.1, BA.1.1, BA.2, BA.3)

Emergence of Omicron

CDC has been using viral genomic surveillance throughout the course of the pandemic to track COVID-19 variants, and inform public health practice.

- **November 24, 2021:** A new variant of COVID-19, B.1.1.529, was reported to the World Health Organization (WHO). This new variant was first detected in specimens collected on November 11, 2021 in Botswana and on November 14, 2021 in South Africa.
- **November 26, 2021:** WHO named the B.1.1.529 Omicron and classified it as a Variant of Concern (VOC).
- **November 30, 2021:** The United States designated Omicron as a Variant of Concern.
- **December 1, 2021:** The first confirmed U.S. case of Omicron was identified.

- **December 21, 2021:** BA.2 was first identified in the United States from a sample collected on December 14, 2021, in New Jersey.

Related Pages

- Symptoms
- Omicron Potential Spread
- Omicron Data
- About Variants

Last Updated Mar. 29, 2022

EXHIBIT “C”

Centers for Disease Control and Prevention

COVID-19 after Vaccination: Possible Breakthrough Infection

Updated June 23, 2022

COVID-19 vaccines help protect against severe illness, hospitalization and death. COVID-19 vaccines also help protect against infection. People who are vaccinated may still get COVID-19. When people who have been vaccinated get COVID-19, they are much less likely to experience severe symptoms than people who are unvaccinated.

> To get the best protection against COVID-19, especially against severe illness and hospitalization, stay up to date on your COVID-19 vaccines.

When someone who is vaccinated with either a primary series or a primary series plus a booster dose gets infected with the virus that causes COVID-19, it is referred to as a "vaccine breakthrough infection."

> When people who are vaccinated get COVID-19 get a breakthrough infection, they are much less likely to experience severe symptoms than people who are unvaccinated.

People who get vaccine breakthrough infections can spread COVID-19 to other people. When a community reports more COVID-19 infections, that means more virus is circulating. When more virus is circulating, more breakthrough infections will occur even when vaccination rates are high. Even if you are vaccinated, if you live in a county with a high COVID-19 Community Level, you and others in your community, whether vaccinated or not, should take more steps to protect yourself and others, like wearing a mask in indoor public places.

CDC monitors reported vaccine breakthrough infections to better understand patterns of COVID-19 among people who are vaccinated and unvaccinated. The latest rates of COVID-19 cases and deaths by vaccination status are available on the CDC COVID Data Tracker.

Learn more about the benefits of COVID-19 vaccines:

- Benefits of Getting a COVID-19 Vaccine
- COVID-19 Vaccines Work

Last Updated June 23, 2022

EXHIBIT “D”

Risk of myocarditis following sequential COVID-19 vaccinations by age and sex

Martina Patone, Xue W Mei, Lahiru Handunnetthi, Sharon Dixon, Francesco Zaccardi, Manu Shankar-Hari, Peter Watkinson, Kamlesh Khunti, Anthony Harnden, Carol AC Coupland, Keith M. Channon, Nicholas L Mills, Aziz Sheikh, Julia Hippisley-Cox

doi: https://doi.org/10.1101/2021.12.23.21268276

ABSTRACT

In an updated self-controlled case series analysis of 42,200,614 people aged 13 years or more, we evaluate the association between COVID-19 vaccination and myocarditis, stratified by age and sex, including 10,978,507 people receiving a third vaccine dose. Myocarditis risk was increased during 1-28 days following a third dose of BNT162b2 (IRR 2.02, 95%CI 1.40, 2.91). Associations were strongest in males younger than 40 years for all vaccine types with an additional 3 (95%CI 1, 5) and 12 (95% CI 1,17) events per million estimated in the 1-28 days following a first dose of BNT162b2 and mRNA-1273, respectively; 14 (95%CI 8, 17), 12 (95%CI 1, 7) and 101 (95%CI 95, 104) additional events following a second dose of ChAdOx1, BNT162b2 and mRNA-1273, respectively; and 13 (95%CI 7, 15) additional events following a third dose of BNT162b2, compared with 7 (95%CI 2, 11) additional events following COVID-19 infection. An association between COVID-19 infection and myocarditis was observed in all ages for both sexes but was substantially higher in those older than 40 years. These findings have important implications for public health and vaccination policy.

Funding Health Data Research UK.

Competing Interest Statement

AS is a member of the Scottish Government Chief Medical Officer's COVID-19 Advisory Group, the Scottish Government's Standing Committee on Pandemics. and AstraZeneca's Thrombotic Thrombocytopenic Advisory Group. All roles are unremunerated. JHC reports grants from National Institute for Health Research (NIHR) Biomedical Research Centre, Oxford, grants from John Fell Oxford University Press Research Fund, grants from Cancer Research UK (CR-UK) grant number C5255/A18085, through the Cancer Research UK Oxford Centre, grants from the Oxford Wellcome Institutional Strategic Support Fund (204826/Z/16/Z) and other research councils, during the conduct of the study. JHC is an unpaid director of QResearch, a not-for-profit organisation which is a partnership between the University of Oxford and EMIS Health who supply the QResearch database used for this work. JHC is a founder and shareholder of ClinRisk ltd and was its medical director until 31st May 2019. ClinRisk Ltd produces open and closed source software to implement clinical risk algorithms (outside this work) into clinical computer systems. JHC is chair of the NERVTAG risk stratification subgroup and a member of SAGE COVID-19 groups and the NHS group advising on prioritisation of use of monoclonal antibodies in SARS-CoV-2 infection. AH is a member of the Joint Committee on Vaccination and Immunisation (JCVI). KK is a member of the Governments Scientific Advisory Group for Emergencies. All other authors declare no competing interests related to this paper.

Clinical Protocols

https://www.qresearch.org/media/1304/ox107_covid_vaccine_safety_protocol.pdf

Funding Statement

Funding: Health Data Research UK.

Author Declarations

I confirm all relevant ethical guidelines have been followed, and any necessary IRB and/or ethics committee approvals have been obtained.

Yes

The details of the IRB/oversight body that provided approval or exemption for the research described are given below:

National Health Service Research Ethics Committee (NHS REC) approval was obtained from East Midlands-Derby Research Ethics Committee [reference 04/03/2021].

I confirm that all necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived, and that any patient/participant/sample identifiers included were not known to anyone (e.g., hospital staff, patients or participants themselves) outside the research group so cannot be used to identify individuals.

Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance).

Yes

I have followed all appropriate research reporting guidelines and uploaded the relevant EQUATOR Network research reporting checklist(s) and other pertinent material as supplementary files, if applicable.

Yes

Paper in collection COVID-19 SARS-CoV-2 preprints from medRxiv and bioRxiv

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Pain Medicine

Palliative Medicine

Pathology

Pediatrics

Pharmacology and Therapeutics

Primary Care Research

Psychiatry and Clinical Psychology

Public and Global Health

Radiology and Imaging

Rehabilitation Medicine and Physical Therapy

Respiratory Medicine

Rheumatology

Sexual and Reproductive Health

Sports Medicine

Surgery

Toxicology

Transplantation

Urology

EXHIBIT “E”

current issues in molecular biology

MDPI

Article

Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line

Markus Aldén [1], Francisko Olofsson Falla [1], Daowei Yang [1], Mohammad Barghouth [1], Cheng Luan [1], Magnus Rasmussen [2] and Yang De Marinis [1,*]

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* Correspondence: yang.de_marinis@med.lu.se

Abstract: Preclinical studies of COVID-19 mRNA vaccine BNT162b2, developed by Pfizer and BioNTech, showed reversible hepatic effects in animals that received the BNT162b2 injection. Furthermore, a recent study showed that SARS-CoV-2 RNA can be reverse-transcribed and integrated into the genome of human cells. In this study, we investigated the effect of BNT162b2 on the human liver cell line Huh7 in vitro. Huh7 cells were exposed to BNT162b2, and quantitative PCR was performed on RNA extracted from the cells. We detected high levels of BNT162b2 in Huh7 cells and changes in gene expression of long interspersed nuclear element-1 (LINE-1), which is an endogenous reverse transcriptase. Immunohistochemistry using antibody binding to LINE-1 open reading frame-1 RNA-binding protein (ORFp1) on Huh7 cells treated with BNT162b2 indicated increased nucleus distribution of LINE-1. PCR on genomic DNA of Huh7 cells exposed to BNT162b2 amplified the DNA sequence unique to BNT162b2. Our results indicate a fast up-take of BNT162b2 into human liver cell line Huh7, leading to changes in LINE-1 expression and distribution. We also show that BNT162b2 mRNA is reverse transcribed intracellularly into DNA in as fast as 6 h upon BNT162b2 exposure.

Keywords: COVID-19 mRNA vaccine; BNT162b2; liver; reverse transcription; LINE-1; Huh7

Citation: Aldén, M.; Olofsson Falla, F.; Yang, D.; Barghouth, M.; Luan, C.; Rasmussen, M.; De Marinis, Y. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line. *Curr. Issues Mol. Biol.* **2022**, *44*, 1115–1126. https://doi.org/10.3390/cimb44030073

Academic Editor: Stephen Malnick

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1. Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was announced by the World Health Organization (WHO) as a global pandemic on 11 March 2020, and it emerged as a devasting health crisis. As of February 2022, COVID-19 has led to over 430 million reported infection cases and 5.9 million deaths worldwide [1]. Effective and safe vaccines are urgently needed to reduce the morbidity and mortality rates associated with COVID-19.

Several vaccines for COVID-19 have been developed, with particular focus on mRNA vaccines (by Pfizer-BioNTech and Moderna), replication-defective recombinant adenoviral vector vaccines (by Janssen-Johnson and Johnson, Astra-Zeneca, Sputnik-V, and CanSino), and inactivated vaccines (by Sinopharm, Bharat Biotech and Sinovac). The mRNA vaccine has the advantages of being flexible and efficient in immunogen design and manufacturing, and currently, numerous vaccine candidates are in various stages of development and application. Specifically, COVID-19 mRNA vaccine BNT162b2 developed by Pfizer and BioNTech has been evaluated in successful clinical trials [2–4] and administered in national COVID-19 vaccination campaigns in different regions around the world [5–8].

BNT162b2 is a lipid nanoparticle (LNP)–encapsulated, nucleoside-modified RNA vaccine (modRNA) and encodes the full-length of SARS-CoV-2 spike (S) protein, modified

by two proline mutations to ensure antigenically optimal pre-fusion conformation, which mimics the intact virus to elicit virus-neutralizing antibodies [3]. Consistent with randomized clinical trials, BNT162b2 showed high efficiency in a wide range of COVID-19-related outcomes in a real-world setting [5]. Nevertheless, many challenges remain, including monitoring for long-term safety and efficacy of the vaccine. This warrants further evaluation and investigations. The safety profile of BNT162b2 is currently only available from short-term clinical studies. Less common adverse effects of BNT162b2 have been reported, including pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia [4,9–20]. There are also studies that report adverse effects observed in other types of vaccines [21–24]. To better understand mechanisms underlying vaccine-related adverse effects, clinical investigations as well as cellular and molecular analyses are needed.

A recent study showed that SARS-CoV-2 RNAs can be reverse-transcribed and integrated into the genome of human cells [25]. This gives rise to the question of if this may also occur with BNT162b2, which encodes partial SARS-CoV-2 RNA. In pharmacokinetics data provided by Pfizer to European Medicines Agency (EMA), BNT162b2 biodistribution was studied in mice and rats by intra-muscular injection with radiolabeled LNP and luciferase modRNA. Radioactivity was detected in most tissues from the first time point (0.25 h), and results showed that the injection site and the liver were the major sites of distribution, with maximum concentrations observed at 8–48 h post-dose [26]. Furthermore, in animals that received the BNT162b2 injection, reversible hepatic effects were observed, including enlarged liver, vacuolation, increased gamma glutamyl transferase (γGT) levels, and increased levels of aspartate transaminase (AST) and alkaline phosphatase (ALP) [26]. Transient hepatic effects induced by LNP delivery systems have been reported previously [27–30], nevertheless, it has also been shown that the empty LNP without modRNA alone does not introduce any significant liver injury [27]. Therefore, in this study, we aim to examine the effect of BNT162b2 on a human liver cell line in vitro and investigate if BNT162b2 can be reverse transcribed into DNA through endogenous mechanisms.

2. Materials and Methods

2.1. Cell Culture

Huh7 cells (JCRB Cell Bank, Osaka, Japan) were cultured in 37 °C at 5% CO_2 with DMEM medium (HyClone, HYCLSH30243.01) supplemented with 10% (*v*/*v*) fetal bovine serum (Sigma-Aldrich, F7524-500ML, Burlington, MA, USA) and 1% (*v*/*v*) Penicillin-Streptomycin (HyClone, SV30010, Logan, UT, USA). For BNT162b2 treatment, Huh7 cells were seeded with a density of 200,000 cells/well in 24-well plates. BNT162b2 mRNA vaccine (Pfizer BioNTech, New York, NY, USA) was diluted with sterile 0.9% sodium chloride injection, USP into a final concentration of 100 µg/mL as described in the manufacturer's guideline [31]. BNT162b2 suspension was then added in cell culture media to reach final concentrations of 0.5, 1.0, or 2.0 µg/mL. Huh7 cells were incubated with or without BNT162b2 for 6, 24, and 48 h. Cells were washed thoroughly with PBS and harvested by trypsinization and stored in −80 °C until further use.

2.2. REAL-TIME RT-QPCR

RNA from the cells was extracted with RNeasy Plus Mini Kit (Qiagen, 74134, Hilden, Germany) following the manufacturer's protocol. RT-PCR was performed using RevertAid First Strand cDNA Synthesis kit (Thermo Fisher Scientific, K1622, Waltham, MA, USA) following the manufacturers protocol. Real-time qPCR was performed using Maxima SYBR Green/ROX qPCR Master Mix (Thermo Fisher Scientific, K0222, Waltham, MA, USA) with primers for BNT162b2, *LINE-1* and housekeeping genes *ACTB* and *GAPDH* (Table 1).

Table 1. Primer sequences of RT-qPCR and PCR.

Target	Sequence
ACTB forward	CCTCGCCTTTGCCGATCC
ACTB reverse	GGATCTTCATGAGGTAGTCAGTC
GAPDH forward	CTCTGCTCCTCCTGTTCGAC
GAPDH reverse	TTAAAAGCAGCCCTGGTGAC
LINE-1 forward	TAACCAATACAGAGAAGTGC
LINE-1 reverse	GATAATATCCTGCAGAGTGT
BNT162b2 forward	CGAGGTGGCCAAGAATCTGA
BNT162b2 reverse	TAGGCTAAGCGTTTTGAGCTG

2.3. Immunofluorescence Staining and Confocal Imaging

Huh7 cells were cultured in eight-chamber slides (LAB-TEK, 154534, Santa Cruz, CA, USA) with a density of 40,000 cells/well, with or without BNT162b2 (0.5, 1 or 2 µg/mL) for 6 h. Immunohistochemistry was performed using primary antibody anti-LINE-1 ORF1p mouse monoclonal antibody (Merck, 3574308, Kenilworth, NJ, USA), secondary antibody Cy3 Donkey anti-mouse (Jackson ImmunoResearch, West Grove, PA, USA), and Hoechst (Life technologies, 34850, Carlsbad, CA, USA), following the protocol from Thermo Fisher (Waltham, MA, USA). Two images per condition were taken using a Zeiss LSM 800 and a 63X oil immersion objective, and the staining intensity was quantified on the individual whole cell area and the nucleus area on 15 cells per image by ImageJ 1.53c. LINE-1 staining intensity for the cytosol was calculated by subtracting the intensity of the nucleus from that of the whole cell. All images of the cells were assigned a random number to prevent bias. To mark the nuclei (determined by the Hoechst staining) and the whole cells (determined by the borders of the LINE-1 fluorescence), the Freehand selection tool was used. These areas were then measured, and the mean intensity was used to compare the groups.

2.4. Genomic DNA Purification, PCR Amplification, Agarose Gel Purification, and Sanger Sequencing

Genomic DNA was extracted from cell pellets with PBND buffer (10 mM Tris-HCl pH 8.3, 50 mM KCl, 2.5 mM MgCl2, 0.45% NP-40, 0.45% Tween-20) according to protocol described previously [32]. To remove residual RNA from the DNA preparation, RNase (100 µg/mL, Qiagen, Hilden, Germany) was added to the DNA preparation and incubated at 37 °C for 3 h, followed by 5 min at 95 °C. PCR was then performed using primers targeting BNT162b2 (sequences are shown in Table 1), with the following program: 5 min at 95 °C, 35 cycles of 95 °C for 30 s, 58 °C for 30 s, and 72 °C for 1 min; finally, 72 °C for 5 min and 12 °C for 5 min. PCR products were run on 1.4% (*w*/*v*) agarose gel. Bands corresponding to the amplicons of the expected size (444 bps) were cut out and DNA was extracted using QIAquick PCR Purification Kit (Qiagen, 28104, Hilden, Germany), following the manufacturer's instructions. The sequence of the DNA amplicon was verified by Sanger sequencing (Eurofins Genomics, Ebersberg, Germany).

Statistics

Statistical comparisons were performed using two-tailed Student's *t*-test and ANOVA. Data are expressed as the mean ± SEM or ± SD. Differences with $p < 0.05$ are considered significant.

2.5. Ethical Statements

The Huh7 cell line was obtained from Japanese Collection of Research Bioresources (JCRB) Cell Bank.

3. Results

3.1. BNT162b2 Enters Human Liver Cell Line Huh7 Cells at High Efficiency

To determine if BNT162b2 enters human liver cells, we exposed human liver cell line Huh7 to BNT162b2. In a previous study on the uptake kinetics of LNP delivery in Huh7 cells, the maximum biological efficacy of LNP was observed between 4–7 h [33]. Therefore, in our study, Huh7 cells were cultured with or without increasing concentrations of BNT162b2 (0.5, 1.0 and 2.0 μg/mL) for 6, 24, and 48 h. RNA was extracted from cells and a real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR) was performed using primers targeting the BNT162b2 sequence, as illustrated in Figure 1. The full sequence of BNT162b2 is publicly available [34] and contains a two-nucleotides cap; 5′- untranslated region (UTR) that incorporates the 5′ -UTR of a human α-globin gene; the full-length of SARS-CoV-2 S protein with two proline mutations; 3′-UTR that incorporates the human mitochondrial 12S rRNA (mtRNR1) segment and human AES/TLE5 gene segment with two C→U mutations; poly(A) tail. Detailed analysis of the S protein sequence in BNT162b2 revealed 124 sequences that are 100% identical to human genomic sequences and three sequences with only one nucleotide (nt) mismatch in 19–26 nts (Table S1, see Supplementary Materials). To detect BNT162b2 RNA level, we designed primers with forward primer located in SARS-CoV-2 S protein regions and reverse primer in 3′-UTR, which allows detection of PCR amplicon unique to BNT162b2 without unspecific binding of the primers to human genomic regions.

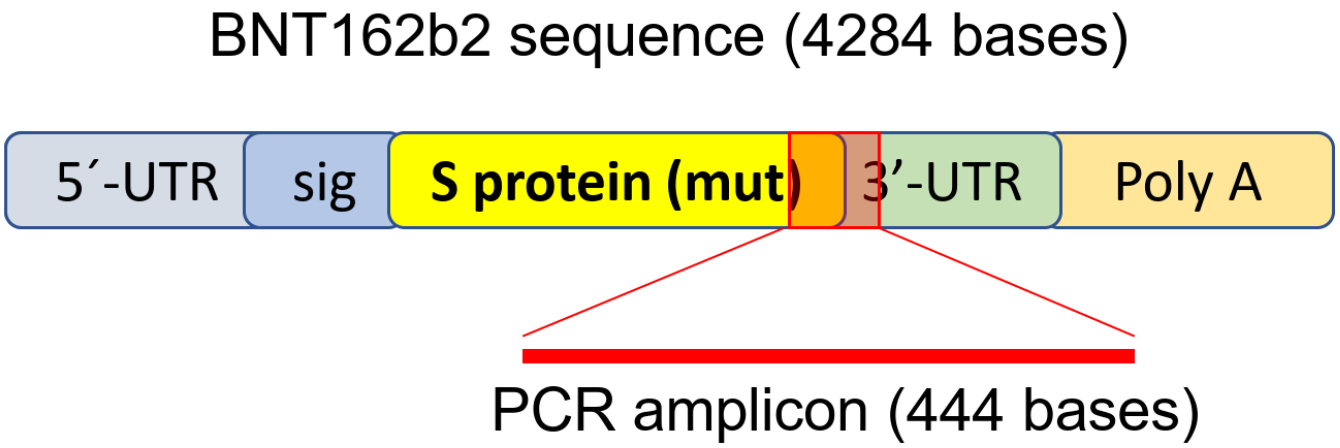

Figure 1. PCR primer set used to detect mRNA level and reverse-transcription of BNT162b2. Illustration of BNT162b2 was adapted from previously described literature [34].

RT-qPCR results showed that Huh7 cells treated with BNT162b2 had high levels of BNT162b2 mRNA relative to housekeeping genes at 6, 24, and 48 h (Figure 2, presented in logged $2^{-\Delta\Delta CT}$ due to exceptionally high levels). The three BNT162b2 concentrations led to similar intracellular BNT162b2 mRNA levels at the different time points, except that the significant difference between 1.0 and 2.0 μg/mL was observed at 48 h. BNT162b2 mRNA levels were significantly decreased at 24 h compared to 6 h, but increased again at 48 h.

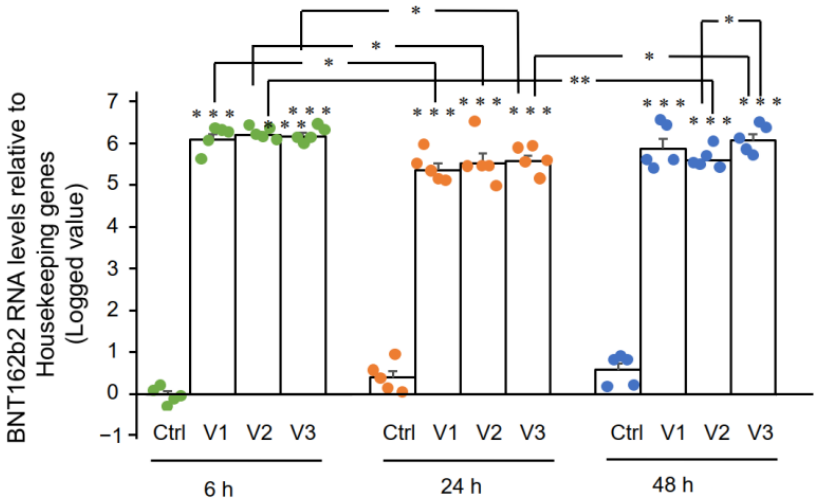

Figure 2. BNT162b2 mRNA levels in Huh7 cells treated with BNT162b2. Huh7 cells were treated without (Ctrl) or with 0.5 (V1), 1 (V2), and 2 µg/mL (V3) of BNT162b2 for 6 (green dots), 24 (orange dots), and 48 h (blue dots). RNA was purified and qPCR was performed using primers targeting BNT162b2. RNA levels of BNT162b2 are presented as logged $2^{-\Delta\Delta CT}$ values relative to house-keeping genes *GAPDH* and *ACTB*. Results are from five independent experiments ($n = 5$). Differences between respective groups were analyzed using two-tailed Student's *t*-test. Data are expressed as the mean ± SEM. (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ vs. respective control at each time point, or as indicated).

3.2. Effect of BNT162b2 on Human Endogenous Reverse Transcriptase Long Interspersed Nuclear Element-1 (LINE-1)

Here we examined the effect of BNT162b2 on *LINE-1* gene expression. RT-qPCR was performed on RNA purified from Huh7 cells treated with BNT162b2 (0, 0.5, 1.0, and 2.0 µg/mL) for 6, 24, and 48 h, using primers targeting *LINE-1*. Significantly increased *LINE-1* expression compared to control was observed at 6 h by 2.0 µg/mL BNT162b2, while lower BNT162b2 concentrations decreased *LINE-1* expression at all time points (Figure 3).

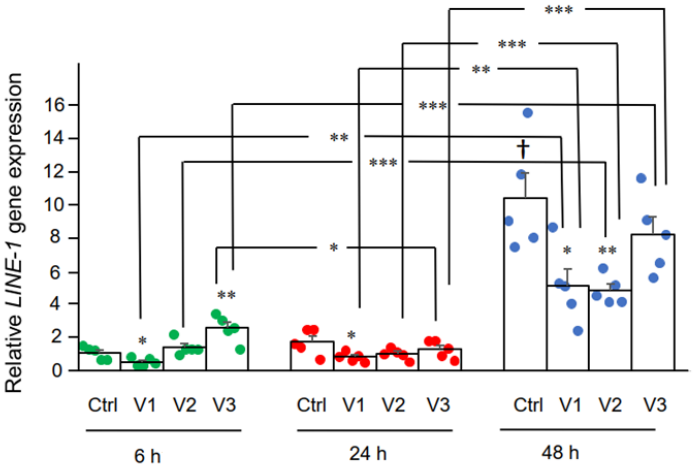

Figure 3. *LINE-1* mRNA levels in Huh7 cells treated with BNT162b2. Huh7 cells were treated without (Ctrl) or with 0.5 (V1), 1 (V2), and 2 µg/mL (V3) of BNT162b2 for 6 (green dots), 24 (red dots), and 48 h (blue dots). RNA was purified and qPCR was performed using primers targeting *LINE-1*. RNA levels of *LINE-1* are presented as $2^{-\Delta\Delta CT}$ values relative to house-keeping genes *GAPDH* and *ACTB*. Results are from five independent experiments ($n = 5$). Differences between respective groups were analyzed using two-tailed Student's *t*-test. Data are expressed as the mean ± SEM. (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ vs. respective control at each time point, or as indicated; † $p < 0.05$ vs. 6 h-Ctrl).

Next, we studied the effect of BNT162b2 on LINE-1 protein level. The full-length LINE-1 consists of a 5′ untranslated region (UTR), two open reading frames (ORFs), ORF1 and ORF2, and a 3′UTR, of which ORF1 is an RNA binding protein with chaperone activity. The retrotransposition activity of LINE-1 has been demonstrated to involve ORF1 translocation to the nucleus [35]. Huh7 cells treated with or without BNT162b2 (0.5, 1.0 and 2.0 µg/mL) for 6 h were fixed and stained with antibodies binding to LINE-1 ORF1p, and DNA-specific probe Hoechst for visualization of cell nucleus (Figure 4a). Quantification of immunofluorescence staining intensity showed that BNT162b2 increased LINE-1 ORF1p protein levels in both the whole cell area and nucleus at all concentrations tested (Figure 4b–d).

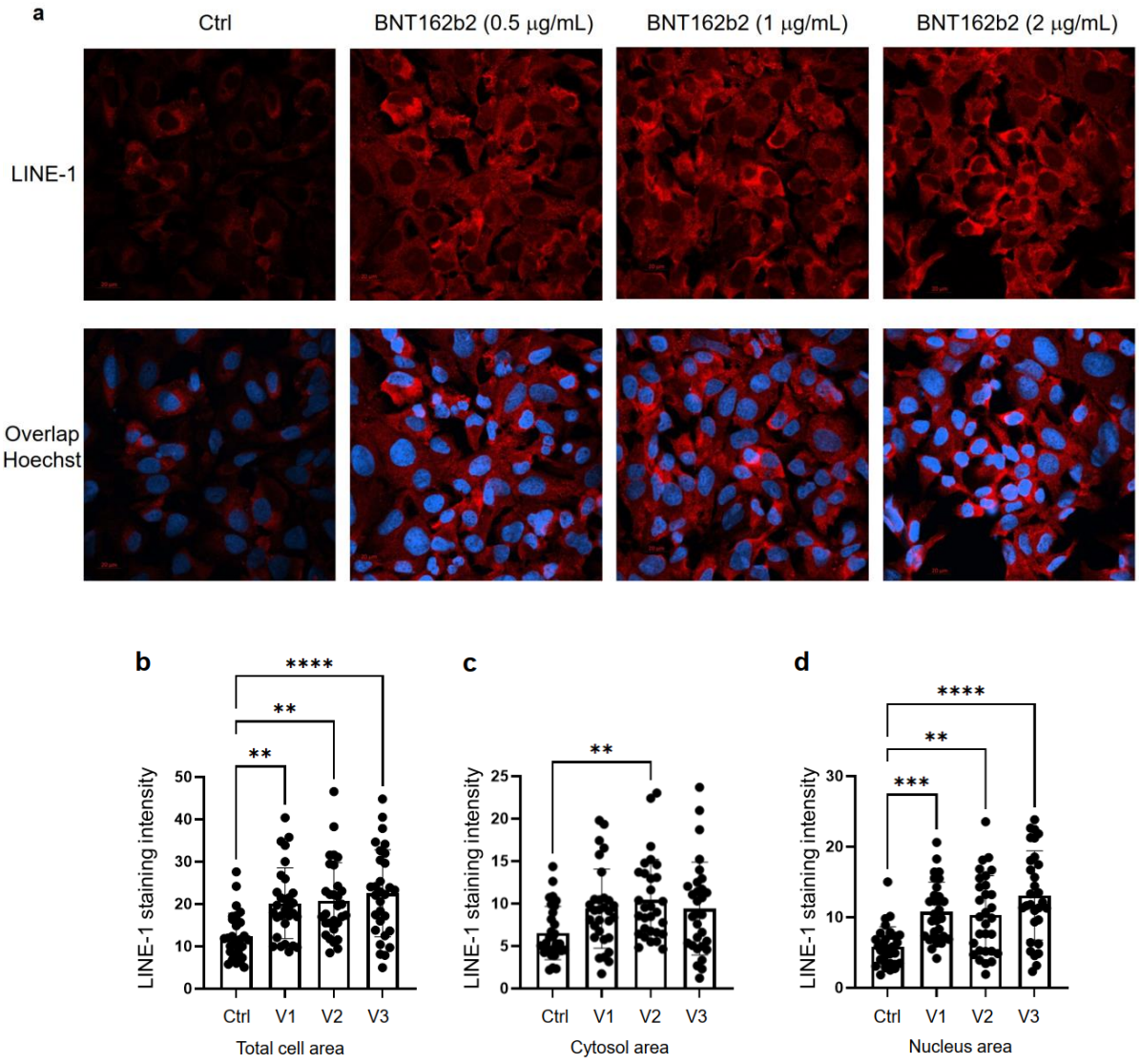

Figure 4. Immunohistochemistry of Huh7 cells treated with BNT162b2 on LINE-1 protein distribution. Huh7 cells were treated without (Ctrl) or with 0.5, 1, and 2 µg/mL of BNT162b2 for 6 h. Cells were fixed and stained with antibodies binding to LINE-1 ORF1p (red) and DNA-specific probe Hoechst for visualization of cell nucleus (blue). (**a**) Representative images of LINE-1 expression in Huh7 cells treated with or without BNT162b2. (**b**–**d**) Quantification of LINE-1 protein in whole cell area (**b**), cytosol (**c**), and nucleus (**d**). All data were analyzed using One-Way ANOVA, and graphs were created using GraphPad Prism V 9.2. All data is presented as mean ± SD (** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$ as indicated).

3.3. Detection of Reverse Transcribed BNT162b2 DNA in Huh7 Cells

A previous study has shown that entry of LINE-1 protein into the nucleus is associated with retrotransposition [35]. In the immunofluorescence staining experiment described above, increased levels of LINE-1 in the nucleus were observed already at the lowest concentration of BNT162b2 (0.5 μg/mL). To examine if BNT162b2 is reversely transcribed into DNA when LINE-1 is elevated, we purified genomic DNA from Huh7 cells treated with 0.5 μg/mL of BNT162b2 for 6, 24, and 48 h. Purified DNA was treated with RNase to remove RNA and subjected to PCR using primers targeting BNT162b2, as illustrated in Figure 1. Amplified DNA fragments were then visualized by electrophoresis and gel-purified (Figure 5). BNT162b2 DNA amplicons were detected in all three time points (6, 24, and 48 h). Sanger sequencing confirmed that the DNA amplicons were identical to the BNT162b2 sequence flanked by the primers (Table 2). To ensure that the DNA amplicons were derived from DNA but not BNT162b2 RNA, we also performed PCR on RNA purified from Huh7 cells treated with 0.5 μg/mL BNT162b2 for 6 h, with or without RNase treatment (Ctrl 5 and 6 in Figure 5), and no amplicon was detected in the RNA samples subjected to PCR.

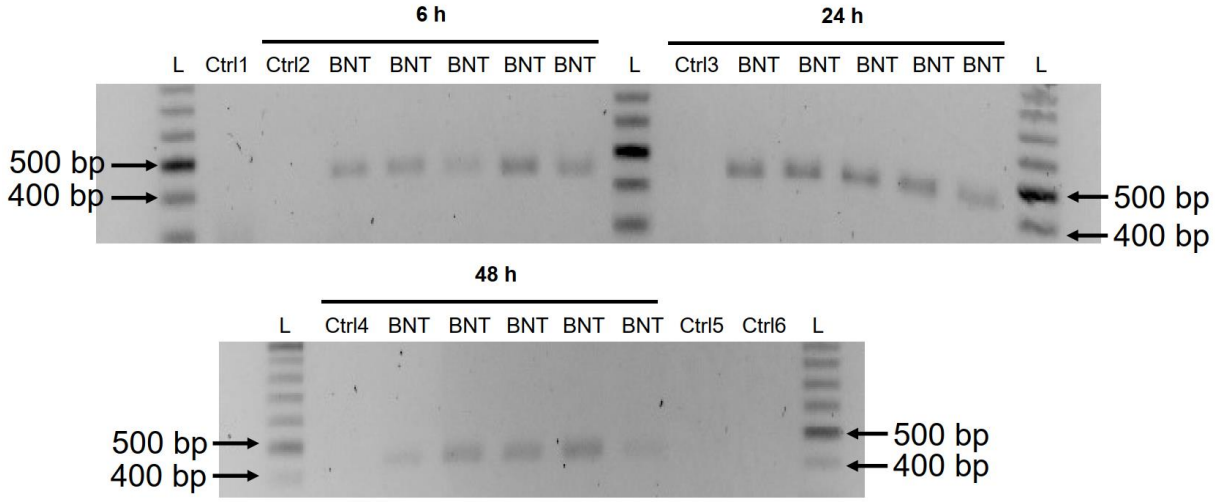

Figure 5. Detection of DNA amplicons of BNT162b2 in Huh7 cells treated with BNT162b2. Huh7 cells were treated without (Ctrl) or with 0.5 μg/mL of BNT162b2 for 6, 24, and 48 h. Genomic DNA was purified and digested with 100 μg/mL RNase. PCR was run on all samples with primers targeting BNT162b2, as shown in Figure 1 and Table 1. DNA amplicons (444 bps) were visualized on agarose gel. BNT: BNT162b2; L: DNA ladder; Ctrl1: cultured Huh7 cells; Ctrl2: Huh7 cells without BNT162b2 treatment collected at 6 h; Ctrl3: Huh7 cells without BNT162b2 treatment collected at 24 h; Ctrl4: Huh7 cells without BNT162b2 treatment collected at 48 h; Ctrl5: RNA from Huh7 cells treated with 0.5 μg/mL of BNT162b2 for 6 h; Ctrl6: RNA from Huh7 cells treated with 0.5 μg/mL of BNT162b2 for 6 h, digested with RNase.

Table 2. Sanger sequencing result of the BNT162b2 amplicon.

CGAGGTGGCCAAGAATCTGAACGAGAGCCTGATCGACCTGCAAGAACTGGGGAAGT
ACGAGCAGTACATCAAGTGGCCCTGGTACATCTGGCTGGGCTTTATCGCCGGACTGATTG
CCATCGTGATGGTCACAATCATGCTGTGTTGCATGACCAGCTGCTGTAGCTGCCTGAAGG
GCTGTTGTAGCTGTGGCAGCTGCTGCAAGTTCGACGAGGACGATTCTGAGCCCGTGCTGA
AGGGCGTGAAACTGCACTACACATGATGACTCGAGCTGGTACTGCATGCACGCAATGCTA
GCTGCCCCTTTCCCGTCCTGGGTACCCCGAGTCTCCCCCGACCTCGGGTCCCAGGTATGC
TCCCACCTCCACCTGCCCCACTCACCACCTCTGCTAGTTCCAGACACCTCCCAAGCACGC
AGCAATGCAGCTCAAAACGCTTAGCCTA

4. Discussion

In this study we present evidence that COVID-19 mRNA vaccine BNT162b2 is able to enter the human liver cell line Huh7 in vitro. BNT162b2 mRNA is reverse transcribed intracellularly into DNA as fast as 6 h after BNT162b2 exposure. A possible mechanism for reverse transcription is through endogenous reverse transcriptase LINE-1, and the nucleus protein distribution of LINE-1 is elevated by BNT162b2.

Intracellular accumulation of LNP in hepatocytes has been demonstrated in vivo [36]. A preclinical study on BNT162b2 showed that BNT162b2 enters the human cell line HEK293T cells and leads to robust expression of BNT162b2 antigen [37]. Therefore, in this study, we first investigated the entry of BNT162b2 in the human liver cell line Huh7 cells. The choice of BNT162b2 concentrations used in this study warrants explanation. BNT162b2 is administered as a series of two doses three weeks apart, and each dose contains 30 μg of BNT162b2 in a volume of 0.3 mL, which makes the local concentration at the injection site at the highest 100 μg/mL [31]. A previous study on mRNA vaccines against H10N8 and H7N9 influenza viruses using a similar LNP delivery system showed that the mRNA vaccine can distribute rather nonspecifically to several organs such as liver, spleen, heart, kidney, lung, and brain, and the concentration in the liver is roughly 100 times lower than that of the intra-muscular injection site [38]. In the assessment report on BNT162b2 provided to EMA by Pfizer, the pharmacokinetic distribution studies in rats demonstrated that a relatively large proportion (up to 18%) of the total dose distributes to the liver [26]. We therefore chose to use 0.5, 1, and 2 μg/mL of vaccine in our experiments on the liver cells. However, the effect of a broader range of lower and higher concentrations of BNT162b2 should also be verified in future studies.

In the current study, we employed a human liver cell line for in vitro investigation. It is worth investigating if the liver cells also present the vaccine-derived SARS-CoV-2 spike protein, which could potentially make the liver cells targets for previously primed spike protein reactive cytotoxic T cells. There has been case reports on individuals who developed autoimmune hepatitis [39] after BNT162b2 vaccination. To obtain better understanding of the potential effects of BNT162b2 on liver function, in vivo models are desired for future studies.

In the BNT162b2 toxicity report, no genotoxicity nor carcinogenicity studies have been provided [26]. Our study shows that BNT162b2 can be reverse transcribed to DNA in liver cell line Huh7, and this may give rise to the concern if BNT162b2-derived DNA may be integrated into the host genome and affect the integrity of genomic DNA, which may potentially mediate genotoxic side effects. At this stage, we do not know if DNA reverse transcribed from BNT162b2 is integrated into the cell genome. Further studies are needed to demonstrate the effect of BNT162b2 on genomic integrity, including whole genome sequencing of cells exposed to BNT162b2, as well as tissues from human subjects who received BNT162b2 vaccination.

Human autonomous retrotransposon LINE-1 is a cellular endogenous reverse transcriptase and the only remaining active transposon in humans, able to retrotranspose itself and other nonautonomous elements [40,41], and ~17% of the human genome are comprised of LINE-1 sequences [42]. The nonautonomous *Alu* elements, short, interspersed nucleotide elements (SINEs), variable-number-of-tandem-repeats (VNTR), as well as cellular mRNA-processed pseudogenes, are retrotransposed by the LINE-1 retrotransposition proteins working in *trans* [43,44]. A recent study showed that endogenous LINE-1 mediates reverse transcription and integration of SARS-CoV-2 sequences in the genomes of infected human cells [25]. Furthermore, expression of endogenous LINE-1 is often increased upon viral infection, including SARS-CoV-2 infection [45–47]. Previous studies showed that LINE-1 retrotransposition activity is regulated by RNA metabolism [48,49], DNA damage response [50], and autophagy [51]. Efficient retrotransposition of LINE-1 is often associated with cell cycle and nuclear envelope breakdown during mitosis [52,53], as well as exogenous retroviruses [54,55], which promotes entrance of LINE-1 into the nucleus. In our study, we observed increased LINE-1 ORF1p distribution as determined by immunohisto-

chemistry in the nucleus by BNT162b2 at all concentrations tested (0.5, 1, and 2 μg/mL), while elevated *LINE-1* gene expression was detected at the highest BNT162b2 concentration (2 μg/mL). It is worth noting that gene transcription is regulated by chromatin modifications, transcription factor regulation, and the rate of RNA degradation, while translational regulation of protein involves ribosome recruitment on the initiation codon, modulation of peptide elongation, termination of protein synthesis, or ribosome biogenesis. These two processes are controlled by different mechanisms, and therefore they may not always show the same change patterns in response to external challenges. The exact regulation of LINE-1 activity in response to BNT162b2 merits further study.

The cell model that we used in this study is a carcinoma cell line, with active DNA replication which differs from non-dividing somatic cells. It has also been shown that Huh7 cells display significant different gene and protein expression including upregulated proteins involved in RNA metabolism [56]. However, cell proliferation is also active in several human tissues such as the bone marrow or basal layers of epithelia as well as during embryogenesis, and it is therefore necessary to examine the effect of BNT162b2 on genomic integrity under such conditions. Furthermore, effective retrotransposition of LINE-1 has also been reported in non-dividing and terminally differentiated cells, such as human neurons [57,58].

The Pfizer EMA assessment report also showed that BNT162b2 distributes in the spleen (<1.1%), adrenal glands (<0.1%), as well as low and measurable radioactivity in the ovaries and testes (<0.1%) [26]. Furthermore, no data on placental transfer of BNT162b2 is available from Pfizer EMA assessment report. Our results showed that BNT162b2 mRNA readily enters Huh7 cells at a concentration (0.5 μg/mL) corresponding to 0.5% of the local injection site concentration, induce changes in LINE-1 gene and protein expression, and within 6 h, reverse transcription of BNT162b2 can be detected. It is therefore important to investigate further the effect of BNT162b2 on other cell types and tissues both in vitro and in vivo.

5. Conclusions

Our study is the first in vitro study on the effect of COVID-19 mRNA vaccine BNT162b2 on human liver cell line. We present evidence on fast entry of BNT162b2 into the cells and subsequent intracellular reverse transcription of BNT162b2 mRNA into DNA.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/cimb44030073/s1.

Author Contributions: M.A., F.O.F., D.Y., M.B. and C.L. performed in vitro experiments. M.A. and F.O.F. performed data analysis. M.R. and Y.D.M. contributed to the implementation of the research, designed, and supervised the study. Y.D.M. wrote the paper with input from all authors. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: All data supporting the findings of this study are available within the article and supporting information.

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Conflicts of Interest: The authors declare no conflict of interest.

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EXHIBIT “F”

WUHAN VIRUS

Former Senior FDA Official: Manufacturers, FDA Negligent In Not Investigating Covid-19 Vaccine Risks To Heart Health

BY: DAVID GORTLER

FEBRUARY 10, 2022

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Manufacturers, FDA, and CDC must investigate serious cardiovascular incidents related to the Pfizer and Moderna Covid vaccines.

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From day one, the U.S. Food and Drug Administration knew the Covid-19 vaccine was linked to serious heart trouble in recipients. The FDA medical officer review of Pfizer's original Covid-19 application notes "clinically important serious adverse reactions [included] anaphylaxis and myocarditis/pericarditis"—that is, severe allergic reactions and inflammation of the heart and or the sac containing the heart, respectively. As of this writing, FDA has not released its review of the Moderna "Spikevax" mRNA vaccine application despite having granted emergency use authorization well more than a year ago and full approval late last month.

The Vaccine Adverse Event Reporting System (VAERS), jointly run by FDA and the Centers for Disease Control, lists a long and impersonal number of cardiovascular-related events in young, healthy people. Without reading the underlying narratives submitted with the reports, it's hard to establish the precise causal links regarding these adverse events. Still, there are thousands of reports of heart attacks, myocarditis, and pericarditis in the United States alone, which *should have* spurred manufacturers and the FDA into full investigation mode.

Studies acknowledged by FDA officials show that the FDA's various safety databases only collect an estimated 1 to 13 percent of all adverse events that occur. Multiple FDA drug safety epidemiologists have stated during official FDA presentation that it only takes a single well-documented adverse event to justify a safety signal investigation and in turn to warn the American public of the potential risk.

Historically, the FDA has sought safety warnings on labels, up to and including a "black boxed warning" and a prescribing restriction known as a Risk Evaluation and Mitigation Strategy (REMS) for much less. For instance, in 2008, after fewer than 200 spontaneous VAERS reports of tendon rupture following administration of the class of antibiotics known as fluoroquinolones, FDA added a "black box warning" and REMS prescribing restrictions.

Yet *thousands* of serious, debilitating, and deadly safety VAERS reports following Covid vaccines and boosters are not being held to the same regulatory standards. If approximately 1 to 13 percent of adverse events are reported, extrapolating those numbers means the actual number of adverse health events could easily be in the hundreds of thousands in the United States and many millions worldwide.

In addition to VAERS, the CDC's Vaccine Safety Datalink indicates an excess risk of myocarditis and pericarditis in recipients following the Pfizer and Moderna vaccines. The cardiovascular risk after any mRNA vaccine is high, but with Moderna it's approximately four times higher than Pfizer's.

Other public health agencies with much tinier budgets and staff compared to our FDA's took action on this *months* ago. In October, Denmark, Finland, Norway, and Sweden suspended the use of the Moderna vaccine for young people, but it's still full speed ahead here in the United States.

Since then, more data has been released affirming the same: On Jan. 25, 2022, a CDC and FDA study published in JAMA shows the risk of myocarditis following any

kind of mRNA Covid vaccination is greater than the background risk in the population, with the largest proportions of cases of myocarditis occurring among white males.

A comprehensive study out of Britain from December 2021 examined data from more than *42 million people* who have taken a Covid-19 shot found a noteworthy increase in myocarditis with mRNA vaccines that persisted and increased with every dose and booster. "An association between Covid-19 infection and myocarditis was observed in all ages for both sexes," the study's abstract states. "These findings have important implications for public health and vaccination policy." Indeed they do—especially in light of the questionable way the FDA approved vaccines in kids from 5 to 13 years old, and the pending FDA applications to approve vaccination in babies starting at 6 months old.

The FDA, CDC, and manufacturers have access to VAERS and additional high-quality denominator-based vaccine safety systems including the Biologics Effectiveness and Safety Initiative (BEST) and the Vaccine Safety Datalink (VSD), respectively. Have manufacturers and our health agencies used these tools and others to fully investigate the cardiovascular health risks of the vaccine? There is reason to doubt, given the political pressure the Biden administration has put on the agencies to advocate for taking the vaccine while almost never mentioning safety.

Myocarditis and pericarditis have historically been rare. They are defined as inflammation of the heart muscle or layers of the pericardial sac, respectively. Both conditions cause easily recognizable ECG changes and have ambiguous symptoms that include shortness of breath and chest pain. Myocarditis and pericarditis can easily be diagnosed clinically with echocardiograms and can be treated by inexpensive pharmacology and bedrest, but for that to happen, people need to know to seek medical diagnosis and care.

Therein is the problem: providers and patients are not being adequately warned to monitor for cardiovascular symptoms despite the increased incidence. Since there is a failure of manufacturers and the FDA to address this and other untoward effects of mRNA utility and mandates, outside drug safety experts need to publicly address mRNA Covid vaccine safety immediately.

On February 4, 2022, a CDC advisory committee proposed extending the gap between Covid-19 shots to mitigate the cardiovascular damage of the vaccine. This indicates the federal government is aware of the serious risk. Yet rather than addressing the risk head-on by communicating the facts to the public, they seem to be taking a "half measure" of changing the interval and hoping to mitigate risk without evidence it will have any effect on outcome.

In the very recent past, anyone warning about *the exact same cardiovascular risk* that this advisory panel spoke about less than a week ago were shamed and banned on social media by "big tech" "fact checkers."

Vaccines are one of the most important inventions in human history, having saved millions of lives. That does not mean every person should get every vaccine. Also, like every drug out there, it is critically important to quickly detect and report safety problems. Now we have a federally mandated vaccine that is clearly no longer effective, and potentially causing additional illness and death.

The failure to adequately monitor and warn for Covid vaccine adverse events has served to harden not only Covid vaccine hesitancy but has shredded the credibility of public health authorities. The failure to openly talk about known adverse reactions erodes trust.

In the 1950s physicians used to not tell patients when they had terminal cancer because they thought it was for their own good. We are long past the day when hiding information from the public is considered good for public health. It never is. It is not only unethical and insulting, it's dangerous.

Dr. David Gortler is a pharmacologist, pharmacist, and an FDA and health policy fellow at the Ethics and Public Policy Center. He was a professor of pharmacology and biotechnology at the Yale University School of Medicine, where he also served at Yale's Bioethicist Center, and was an FDA medical officer who was later appointed by the White House as senior advisor to the FDA commissioner for drug safety, FDA science policy, and FDA regulatory affairs. He is a columnist at Forbes, where he writes on drug safety, health care and FDA policy.

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